Clinical Features and Management of Equine Postoperative Ileus (POI)

Clinical Features and Management of Equine Postoperative Ileus (POI): Survey of Diplomates of the American Colleges of Veterinary Internal Medicine (ACVIM), Veterinary Surgeons (ACVS) and Veterinary Emergency and Critical Care (ACVECC)

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Ethical considerations: The University of Edinburgh School of Veterinary Medicine Ethical Review Committee approval was sought and granted for this study; the only potential ethical issues that this study might have raised laid in the proprietary information about the participants and data protection. To palliate to this, the researchers have ensured that the data collected from the survey were encrypted and remained anonymous.

Competing interests: No competing interest is to be reported.

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Owner informed consent: N/A: See ethical considerations above. This study surveyed clinicians regarding their perceptions and experiences with equine postoperative ileus; as such it did not examine individual case details/records and accordingly owner informed consent was not applicable.

Summary:

Reasons for performing the study: A recent survey of European Colleges (ECEIM and ECVS) revealed the different strategies implemented by, and some of the challenges facing, European clinicians presented with cases of POI. It was concluded that further comparative analysis of opinions, canvassed from additional colleges of equine veterinary specialism worldwide, would provide valuable additional insight into current POI knowledge on a more global scale.

Objectives: To report and compare the current strategies favoured by American veterinary specialists when managing postoperative ileus (POI) in horses that underwent emergency colic surgery.

Methods: Electronic invitations were sent to 814 Large Animal specialists, including 3 colleges: the ACVIM, the ACVS and the ACVECC.

Results: The response rate was 14% (115/814). The most common prevalence range of POI reported was 11 to 20%. The presence of reflux on nasogastric intubation was the main criterion used to define POI. A lesion involving the small intestine was considered the main risk factor for POI. Anti-inflammatory drugs, intravenous fluids and antimicrobial drugs were the primary strategies used when managing POI. Flunixin meglumine and intravenous (IV) lidocaine were the drugs most commonly used in the treatment of horses with POI. Supplementary management strategies targeted mainly the prevention of postoperative adhesions, infection and inflammation.

Conclusions: There is a lack of consensus on the clinical definition of POI. Prospective and objective clinical assessment of the effectiveness of the different strategies contained

79 within this and the European survey is necessary in order to identify a standardized
80 approach to the management of equine POI.

Introduction:

This study constitutes an extension of work, previously targeting specialist European equine veterinary clinicians (ECVS and ECEIM diplomates)[1], which investigated the different strategies used to define, prevent, and treat equine POI and the variation in awareness of the published risk factors for this condition. A general article detailing that original survey was published in 2014 in the Equine Veterinary Journal[1]. The data derived from that original study revealed valuable information on the different strategies implemented by, and some of the challenges facing, European clinicians presented with cases of POI. It was concluded that further comparative analysis of opinions, canvassed from additional colleges of equine veterinary specialism worldwide, would provide valuable additional insight into current POI knowledge on a more global scale.

This survey was aimed at identifying and assessing the opinions and practices of specialist American equine veterinary clinicians in relation to POI. The principal areas which were investigated included the following: (a) an assessment of respondents' awareness of underlying pathophysiological mechanisms and associated risk factors; (b) estimated incidence of POI; (c) the adopted clinical definitions; (d) preferred pharmacological and non-pharmacological management strategies.

This study also permitted a more detailed assessment of opinions relating to certain factors previously identified in the European survey[1] which were considered to be important contributors to POI prevention, diagnosis and treatment.

When considered in isolation, the data derived from this survey provides an overview of the opinions and practices of American equine specialists. When compared with the

103 results of the European[1] survey, it highlights specific areas of commonality and
104 heterogeneity in those opinions and practices. When combined with the results of the
105 European survey, it provides a robust international perspective on the opinions and
106 practices of equine veterinary specialists.

107

108 **Material and methods**

109 Ethical approval for this study was granted by the University of Edinburgh, School of
110 Veterinary Medicine Ethical Review Committee.

111 The original European survey's questionnaire was tested with 3 American surgeons and
112 internists. Minor adjustments were implemented and consisted mainly of adapting certain
113 medication nomenclature from the European to the American practice environment (e.g.
114 lignocaine to lidocaine). The questionnaire (see Supplementary Information) consisted of
115 27 open-ended (e.g. comments, descriptions) and closed (e.g. Likert scales, multiple
116 choices) questions and was designed to permit completion within a period of 10-15
117 minutes. The questions addressed the same general items as in the original European
118 survey.

119 The survey was integrated in a web-based proprietary software[a] program. An invitation to
120 participate was sent by e-mail to 814 Large Animal specialist veterinary clinicians,
121 Diplomates of one (or two) of the, following 3 colleges: the ACVIM (n=531), ACVS
122 (n=283) and the ACVECC (n=43; all with dual membership of either ACVIM or ACVS).

First, second and third reminders were sent at 2 weekly intervals if a response was not obtained. Responses were included in this report only if the questionnaire was fully completed within an 8-week period.

Statistical analysis was generated from the online survey software program[a]. These included respondent numbers, percentages and frequency tables. Some common themes were identified based on the responses provided to specific open questions. The most common comments originating from the open ended questions were categorized and tabulated in the results section. Unless stated otherwise, the percentages expressed in the results reflected the proportion of the total number of responses obtained and were rounded up to the nearest whole number.

Results

Respondent data and practice demographics: Responses were obtained from 115 out of the 814 invited participants (response rate = 14%). These comprised those with sole ACVS (n=55) or ACVIM membership (n=44) and those with dual ACVIM and ACVS (n=1), ACVIM and ACVECC (n=4) and ACVS and ACVECC (n=11) membership. The median range of annual equine caseload at the respondents' clinic was between 2001-3000 cases. Almost a third of respondents (29%) reported between 300 and 399 combined medical and surgical colic cases *per annum*. The number equine colic surgery *per annum* was almost evenly divided between the six different categorical answer options from 1-20 to > 100 (see Supplementary Information, Figure 1).

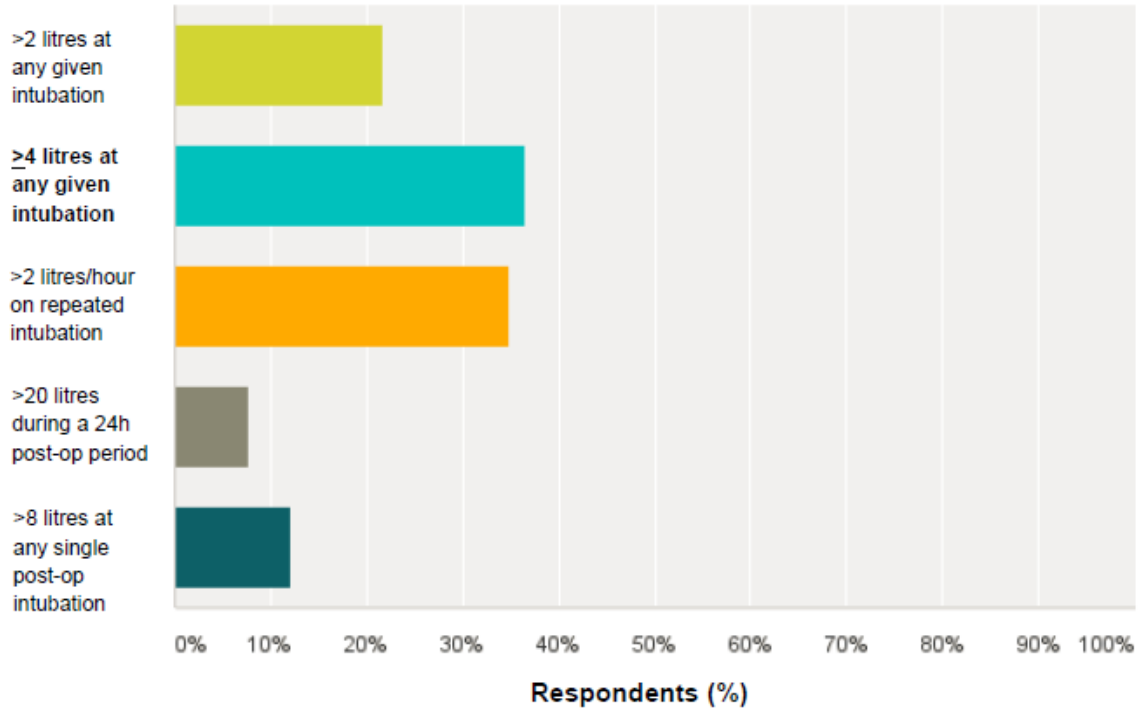
Estimated POI prevalence and definition criteria: Sixty eight per cent of respondents (68%) estimated the prevalence of POI following colic surgery at their respective clinics to be in the range of 0-20%. There were fewer than 5% of respondents reporting a prevalence of POI > 40% (See Supplementary Information, Figure 2). Sixty four percent of respondents (64%) '*do not'* use a hospital/practice protocol for the definition of POI. Ninety-four percent (94%) of respondents considered that presence of reflux on nasogastric intubation was extremely important in classification of a horse having POI (Table 1), with volumes of ≥ 4 litres at any given intubation (37% of respondents) and >2 litres/hour on repeated intubations (35% of respondents) representing the most commonly applied criteria with respect to POI definition (Figure 1).

Table 1: ACVS, ACVIM and ACVECC Diplomates' rating of the importance of different parameters in the diagnostic classification of POI from an online questionnaire of the Clinical Features and Management of Equine POI, completed by 115 respondents

Diagnostic classification of POI parameter	'% 'Extremely Important'	% 'Quite Important'	% 'Not very Important'	% 'Not important at all'
Presence of reflux on nasogastric intubation	**94**	6	0	0
Ultrasonographic evidence of multiple fluid distended SI bowel loops	**67**	28	3	2
Evidence of multiple fluid distended SI loops on rectal examination	**45**	45	10	0
Mild to moderate signs of abdominal discomfort	28	**48**	24	2
Deterioration of cardiac parameters (tachycardia)	21	**48**	28	2
Ultrasonographic evaluation of the motility of other SI parts	38	**42**	19	3
Ultrasonographic evaluation of duodenal motility	29	**41**	26	4
Fever	4	17	**59**	22
Absence of GI sounds	12	39	**43**	6

Bolded: Most common answer

158 **Figure 1:** ACVS, ACVIM and ACVECC Diplomates' postoperative reflux volume corresponding most to
159 respondents' own working definition of POI from an online questionnaire of the Clinical Features and
160 Management of Equine POI completed by 115 respondents



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Perceived risk factors: A lesion involving the small intestines (SI) (70% of respondents) was considered '*extremely important'* as a pre- and intra-operative risk factor for developing POI (Table 2) with the presence of SI distension (69% of respondents) and inflammation (57%) considered the most important postoperative risk factors (Table 3).

Table 2: ACVS, ACVIM and ACVECC Diplomates' rating of the importance of potential pre- and intra-operative risk factors for the development of POI from an online questionnaire of the Clinical Features and Management of Equine POI, completed by 115 respondents

Pre- and intra-operative risk factors	% 'Extremely Important'	% 'Quite Important'	% 'Not very Important'	% 'Not important at all'
Lesions involving the SI	**70**	27	3	0
Intestinal resection and anastomosis	**64**	29	7	0
Degree of bowel distension at surgery	**62**	36	3	0
Increased amount of bowel handling	**60**	33	7	0
Presence of discolored bowel at surgery	**52**	41	7	0
Endotoxaemia (clinical or lab evidence of)	29	**61**	11	0
Increased blood lactate level pre-op	15	**57**	25	4
Increased packed cell volume (PCV) at admission	10	**48**	36	6
Long anaesthesia and surgery duration	35	**46**	19	0
Abnormal bowel motility observed at surgery	34	**45**	20	1
Long-time between referral and admission of colic case	36	**43**	18	3
Administration of opioids as pain medication	4	13	**54**	29

Bolded: Most common answer

178 **Table 3: ACVS, ACVIM and ACVECC Diplomates' rating of the importance of potential**
179 **postoperative risk factors for the development of POI from an online questionnaire of the Clinical**
180 **Features and Management of Equine POI, completed by 115 respondents**

Postoperative risk factors	% 'Extremely Important'	% 'Quite Important'	% 'Not very Important'	% 'Not important at all'
SI distention	**69**	31	0	0
Inflammation	**57**	40	3	0
Abdominal pain	21	**61**	17	2
Interval to commencement of post-op feeding	16	**50**	30	6
Gastric distention	27	**47**	26	0
Postoperative adhesions	35	**46**	18	2
Infection	29	**42**	29	2
Leaving NG tube indwelling	7	25	**59**	8
Volume and type of intravenous fluids given	5	28	**57**	10
Postoperative pain medication (opioids)	7	25	**57**	11
Interval to commencement of post-op exercise	5	28	**53**	13

181 **Bolded:** Most common answer

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183 *Preventive strategies:* Approximately half of respondents (52%) stated that their
184 hospital/practice used a defined protocol in an attempt to prevent POI intra- and
185 postoperatively. Anti-inflammatory drugs (99% of respondents), intravenous fluids
186 (92%), antimicrobial drugs (87%), electrolyte supplementation of fluids (68%), early
187 exercise (47%) and early feeding (32%) were the most commonly employed POI
188 preventive strategies *'in all surgical colic cases',* whereas over half (56%) of respondents
189 stated that opioid administration was used '*only in the minority of cases considered at*
190 *risk for POI*'. Flunixin meglumine (72% of respondents '*in all surgical colic cases'*) and

intravenous (IV) lidocaine (40% *'in all surgical colic cases considered at risk for POI'*) were the drugs most commonly used intra-operatively in surgical colic cases to prevent POI. Similarly, flunixin meglumine (87% *'in all surgical colic cases'*) and IV lidocaine (57% '*in all surgical colic cases considered at risk for POI'*) were the drugs most commonly used postoperatively in surgical colic cases to prevent POI. Although 31% of respondents used polymixin B postoperatively '*in the majority of cases considered at risk for POI',* the same percentage (31%) only used this approach *'in the minority of surgical colic cases considered at risk for POI'*. Similarly, metoclopramide (53%), butorphanol (46%), xylazine (44%) and plasma containing anti-lipopolysaccharide (LPS) antibodies (37%) were mostly used postoperatively *'in the minority of surgical colic cases considered at risk for POI'*.

Treatment strategies: Just over half of the respondents (55%) followed a hospital/practice protocol for the treatment of surgical cases that developed POI. When asked about the pharmacological management of such cases, the respondents again favored flunixin meglumine (77%) and IV lidocaine (69%) '*in all POI cases'*. In comparison, metoclopramide (57%), butorphanol (50%), heparin (49%), plasma containing anti –LPS (43%) and polymyxin B (41%) were the most common choices '*in a few POI cases'*.

The majority of respondents (90%) favored flunixin meglumine as their nonsteroidal anti-inflammatory drug of choice. Forty six percent of these respondents (36/78) specified a dosage of 1.1 mg/kg IV, and 33% (26/78) administered at this dose rate twice daily. Other dose rates used included 0.5 mg/kg IV (14%, 11/78) and 0.25 mg/kg IV (9%, 7/78), at varying frequencies (twice, three or four times daily).

When asked about their favored dosage regimen when using lidocaine in the postoperative treatment of POI cases, most of the 115 respondents commented: 1.3mg/kg bolus followed by a constant rate infusion (CRI) rate of 0.05 mg/kg/min (60%); a lower proportion (11%) used the same CRI rate but '*with no loading dose'*. Twelve per cent of the respondents (12%) mentioned that they use IV lidocaine '*as indicated/published'*.

Supplementary strategies: Comments about supplementary strategies used to avoid or minimise exposure to intra-operative risk factors for POI or other colic surgery-related complications included the prevention of postoperative adhesions (105 comments), infection (77 comments) and inflammation (62 comments). Adhesion prevention protocols included the use of intra-abdominal carboxymethylcellulose (59% of comments, 62/105), abdominal lavage ± heparin (39%, 41/105) and careful/minimal manipulation of the bowel (9%, 10/105). Infection prevention protocols included the use of systemic antimicrobials (61% of comments, 47/77) and abdominal lavage with antimicrobial-containing fluids (34%, 26/77). Comments about inflammation prevention protocols included the use of anti-inflammatory drugs (44% of comments, 25/62); specifically flunixin meglumine (35%, 22/62), careful handling/surgical technique (13%, 8/62), IV lidocaine (11%, 7/62) and dimethyl sulfoxide (DMSO), (10%, 6/62).

The supplementary postoperative strategies utilized to prevent and manage POI were, in decreasing order of frequency: gastric decompression via nasogastric intubation (86% of respondents), judicious timing of feeding (85%), hand-walking exercise (84%), use of antibiotics (83%), control of endotoxaemia (76%), fluid therapy (69%) and other strategies (26%). In relation to gastric decompression via nasogastric intubation of POI cases, 58% of respondents left the tube indwelling; although 57% (38/66) of those

commented that it was *'case dependent'* and 41% (27/66) mentioned: *'only if the patient is refluxing'*.

When asked to comment further on the 'judicious timing of feeding', most of the respondents (85%, 98/115) stated: 'start slowly/in small quantities' (32%, 31/98)**,** 'within 24 hours postoperatively' (29%, 28/98), **'**grazing/grass is best' (28%, 27/98), 'feeding as soon as possible' (21%, 20/98), 'feed when no more reflux' (12%, 12/98) and 'place hay net outside the stall' (11%, 11/98). More detailed comments relating to the introduction of hand-walking exercise (97) included: 'as soon as possible along with early feeding' (28%, 27/97), 'within 24 hours postoperatively' (24%, 23/97), 'implemented routinely' (10%, 10/97) and 'start 2 days postoperatively' (9%, 9/97).

Fluid therapy and parenteral nutrition: In POI cases, the majority of respondents (67%) opted for the administration of fluid therapy at maintenance rates and most (59%) used polyionic resuscitation fluids '*in all POI cases'*. The most common intravenous fluid supplements used in cases that have developed POI were: calcium (64% of respondents) and potassium (64%) *'routinely'* and magnesium (60%) *'depending on clinical pathology results'*. In POI cases, 52% of respondents used total parenteral nutrition (TPN) '*only in a few cases'*, 46% of respondents '*never'* used TPN and 67% used partial parenteral nutrition (PPN), but only '*in a few cases'*. Of the 48 comments relating to the use of TPN and PPN, 88% (42/48) included the use of dextrose, 67% (32/48) the addition of amino acids and, 23% (11/48) mentioned the high cost limitations of such therapy.

Repeat surgery: In POI cases, the majority of respondents (91%) said they would consider a second laparotomy. Of those respondents, 38% (40/104) expressed their

preferred inter-operative time interval to be 2 to 4 days, closely followed by 4-6 days (29%, 30/104).

Discussion

This survey is based on the opinions of 115 Diplomates of three American veterinary medicine and surgery colleges on the description, prevention and treatment of equine POI. With the aim to include as many specialist opinions as possible, the population's criteria for this study consisted of all Diplomates of the ACVS, ACVIM and ACVECC listed under large animal (LA). Although our response rate may be considered low, a significant proportion of contacted Diplomates would be ineligible for our study. Despite recognising that the survey's specific theme (i.e. POI following emergency colic surgery) would render a proportion of the 814 Diplomates ineligible, no alternative means were implemented in order to specifically focus on eligible Diplomates. Hence, in addition to eligible surgeons and clinicians that failed to respond, the non-responders for this study may have included farm animal specialists, field-service or general practitioners, orthopaedic surgeons, and diplomates with a primarily research-based career. The absolute number of respondents from this current survey (115: 67 ACVS + 48 ACVIM) was comparable with similar published surveys and target audiences; e.g. Lefebvre *et al.* 2014 survey (100 respondents from the ECVS and ECEIM; 30% response rate) and the Van Hoogmoed 2004 survey (58 respondents from the ACVS; 52% rate) [1,2].

Consequently, it could be argued that the responses obtained were not representative of the entire population surveyed but rather represent the opinions of a subgroup of

280 veterinary clinicians and surgeons actively involved in equine abdominal surgery and
281 POI management.

282 Comparisons made between the American and European[1] surveys largely revealed a high
283 level of agreement in the responses obtained which further highlighted a number of areas
284 in which there is potential for improvement in the understanding and knowledge of
285 equine POI.

286 Firstly, the most commonly estimated POI prevalence range in both surveys (European -
287 71%; American - 68%) was 0 to 20%. This "estimated" prevalence range falls within the
288 lower ranges of "measured" prevalence derived from various other studies (i.e. 10%-
289 50%) [2,3,4,5]. Although this finding could indicate a decline in incidence of POI it may
290 also reflect inaccuracies in the prevalence estimates provided by the respondents.

291 Then, there was inconsistency among respondents with regard to the specific criteria used
292 to define POI. Although the presence of gastric reflux was still regarded as the most
293 important criterion for defining POI[6,7], there was variation amongst respondents in
294 relation to the volume and rate of yield of fluid considered to be diagnostic. Similar to the
295 European study[1], almost three quarters of respondents applied the criteria of either $\geq$ 4
296 litres at any given intubation or a rate of >2 litres/hour on repeated intubations, with
297 almost one quarter applying the criterion of > 2 litres at any given intubation. Matter-of-
298 factly, the latter criterion was applied by 34% (13/38) of the respondents who reported an
299 estimated prevalence rate >20%, a finding which may highlight the significant influence
300 of varied POI definition criteria on reported prevalence.

Also, the pre-, intra- and postoperative factors considered as *'extremely important'* with respect to their contribution to POI were identical to those identified in the European study[1], indicative of a general awareness of the risk factors published in the veterinary literature [1,3,8,9,10,11]. Likewise, the administration of opioids as an analgesic in the pre- and/or intra-operative as well as in the postoperative periods was largely perceived as *'not very important'* in both studies with respect to its contribution to POI. Moreover, this survey also demonstrated overall support amongst clinicians for the development and use of general 'in-house' guidelines for perioperative care strategies aimed at preventing and treating POI, similar to those applied in human medicine[12].

There was also agreement between studies in relation to the preferred drugs of choice. Both survey studies, and that of Van Hoogmoed *et al.* (2004), identified IV lidocaine as the most common prokinetic drug of choice, with relative consistency in the dosage regimen used[1,2]. Similarly, both studies identified metoclopramide as the second most common prokinetic drug of choice for either intra-operative preventive or postoperative therapeutic use, a finding in contrast to the results of the Van Hoogmoed *et al.* (2004) survey[2], whereby erythromycin lactobionate was the second most popular choice. Although both studies identified lidocaine and flunixin as the 2 most popular drugs for the prevention and treatment of POI, when compared to the European survey (IV lidocaine 78% vs flunixin 78%), IV lidocaine appeared to be less popular (68%) relative to flunixin (77%) in the American survey for the treatment of POI cases. The use of flunixin concurs with the general perception amongst both European and American respondents that inflammation is an *'extremely important'* postoperative risk factor for the development of POI, second only to the presence of SI distension. This likely reflects

an awareness of the increasing body of published evidence supporting a pivotal role for inflammation in equine POI pathogenesis[3,13,14,15,16]. Similarly, it is likely that the reported anti-inflammatory effects of lidocaine [17,18,19], in addition to its perceived prokinetic effects[2], also contributed to the high frequency with which this drug was used, both intra- and postoperatively. Furthermore, in addition to inflammation, pain is recognised as an important risk factor for POI in both humans and horses[1,2,6,9,12,19]. The specific reasons why flunixin was the preferred non-steroidal anti-inflammatory drug (NSAIDs) remain uncertain; however, its reportedly greater potency against the systemic effects of endotoxaemia[17], compared with other NSAIDs, may be a contributing factor in light of the respondents perception that endotoxaemia was "*quite important*" as a risk factor for the development of POI.

Despite the many similarities in results between the European and American surveys, there were certain areas where the responses differed. Firstly, although anti-inflammatory drugs were selected in both surveys as those most commonly used for POI prevention/management, in the American survey they were followed in decreasing frequency of use by intravenous fluid administration, antimicrobial drugs and electrolyte supplementation; whereas, in the European study, they were followed by antimicrobial drug administration and, to a lesser extent, prokinetic drugs[1]. Secondly, the American survey revealed a tendency for clinicians to retain an indwelling nasogastric tube after surgery (58% of respondents), although further comments clarified that this decision was case-dependant, e.g. only if the patient is refluxing or according to clinical signs. In comparison, the majority of European respondents (70%) preferred to pass the nasogastric tube only as required[1]. Thirdly, despite the American survey revealing that

parenteral nutrition was used '*only in a few POI cases'*, in such cases, approximately half and two thirds of the respondents stated that they would use TPN and PPN, respectively. This is in contrast to the European survey[1] in which approximately half of the respondents stated that they would consider the use of PPN '*only in a few POI cases*' and almost three quarters of respondents stated that they would "*never use TPN*". Lastly, despite an almost identical proportion of respondents from each survey stating that they would consider a repeat laparotomy in refractory cases (European - 88% vs American - 91%), a comparatively lower proportion of respondents in the American survey (38%), relative to the European survey (46%) opted for 2 to 4 days and a comparatively higher proportion of respondents in the American survey (29%) relative to the European survey (15%) opted for 4-6 days as the preferred timing of the second surgery relative to the first. The specific reasons for these apparent geographical differences remain unclear; however, it is possible that they are largely attributable to factors such as financial constraints and the presence of established practice policy. However the authors can find no evidence base within the veterinary literature which will preferentially support one approach over another.

The analysis of data derived from this survey of Equine Veterinary Diplomates of American Colleges has provided an overview of the commonly held perceptions related to various aspects of equine POI. Furthermore, comparative analysis has confirmed that the opinions and practices of clinicians in America and Europe are generally very similar and largely informed by knowledge of the relevant veterinary literature. However, the survey results have also helped to confirm that a universal approach to the management of POI does not exist and significant variation remains in relation to some of the

preventative and therapeutic practices being adopted. It should be emphasized that these results are only a measure of current practice and opinions and does not provide evidence about best practice. Further research into ways in which POI can be prevented or attenuated is essential. Recognition of these areas of research is the first step in identifying and prioritising specific areas which may benefit from future study.

Footnote list:

[a] Survey Monkey® , Palo Alto, California, USA.

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Supplementary Information

Figure 1: ACVS, ACVIM and ACVECC Diplomates' approximate annual number of colic surgeries in practice from an online questionnaire of the Clinical Features and Management of Equine POI completed by 115 respondents

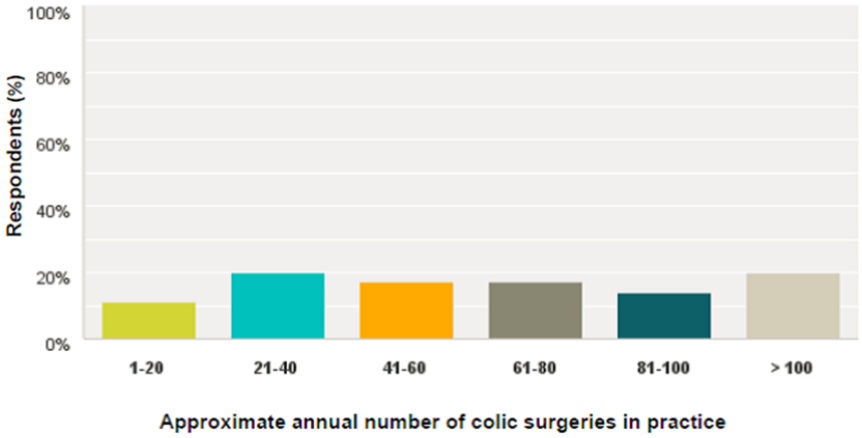

Figure 2: ACVS, ACVIM and ACVECC Diplomates' estimated incidence (%) of POI cases in practice from an online questionnaire of the Clinical Features and Management of Equine POI, completed by 115 respondents